Doxycycline or Oral Corticosteroids for Nasal Polyps

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Therapeutic Options Beyond our Pages highlights randomized controlled trials published in other journals of novel therapeutic options for the conditions treated by allergist-immunologists. Generally written by Editorial Board members with relevant expertise, this feature summarizes the methods and results of the study and then provides the author's perspective regarding the practical use of the information at this time.

The study by Van Zele et al[1] reports positive results for either 20 days of doxycycline (200 mg the first day, followed by 100 mg daily) or 20 days of a tapering schedule of methylprednisolone (32 mg on days 1-5; 16 mg on days 6-10, and 8 mg days 11-20) for the treatment of nasal polyps in a randomized, double-blind, placebo-controlled trial. The primary end point was reduction in nasal polyp score, which was graded 0 to 4 on each side, resulting in a score range of 0 to 8; the score was determined at baseline and weeks 1, 2, 4, 8, and 12. Entry criteria required that the patient either have recurrent polyps after surgery or massive polyps (grade 3 or 4); the total polyp score in each of the 3 groups averaged approximately 6. The patient population in this study was, therefore, at the severe end of the spectrum; results may not be generalizable to patients with milder disease.

This trial of 47 patients reported a significant reduction in endoscopically graded polyp size in both the doxycycline- and methylprednisolone-treated groups compared with placebo. As has been reported by others,[2] the patients who received a burst of methylprednisolone enjoyed a substantive, statistically significant reduction in nasal polyp size (maximum decrease of 2.3 on the 8-point scale); unfortunately, the effect was transient with return to baseline score by week 8. In contrast, the doxycycline-treated group had a less impressive but still statistically significant reduction (maximum decrease of 0.7) in nasal polyp score that persisted through the end of the study, week 12. As the researchers noted, the magnitude of polyp reduction in the doxycycline group is similar to that reported after 4 weeks of treatment with mometasone furoate.[3]

Relative to the secondary outcome of important nasal symptoms, the methylprednisolone group had reduction of postnasal drip, smell loss, and nasal congestion, whereas the doxycycline-treated group improved only in postnasal drip. Neither group showed improvement in anterior rhinorrhea. Improvement in both treatment groups was also seen in the secondary outcome of nasal peak inspiratory flow, with the methylprednisolone group being better than the doxycycline group. Inflammatory markers were measured in nasal secretions. Compared with placebo, both groups had reduced eosinophilic cationic protein (ECP); the methylprednisolone group had reduced IgE and IL-5, whereas the doxycycline group had reduced myeloperoxidase and matrix metalloproteinase-9. One important aspect of the study design to note is that supplemental antibiotics, nasal steroids, and oral glucocorticosteroids were disallowed during the study. Therefore, in some nasal secretion biomarker comparisons, such as ECP, IL-5, and IgE, the differences observed were partly because of increases in the placebo group that occurred because they discontinued nasal steroids.

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The study by Van Zele et al[1] provides category I evidence in support of an oral glucocorticosteroid burst for improvement in the signs and symptoms of nasal polyps. Because of the side effect profile of oral glucocorticosteroids, however, the frequency with which they can be judiciously administered is limited. It should be emphasized that this is probably the first study to evaluate the duration of the effect of a short course of oral glucocorticosteroids. Unfortunately, the effect is transient, essentially disappearing by 8 weeks after initiation of therapy. In practice, most patients prescribed a short course of oral glucocorticosteroids would also be using nasal steroids, which was not the case in this study. It is possible that the effect would have been longer lasting if nasal steroids were concomitantly administered.

This study also provides proof of concept for use of doxycycline in the treatment of nasal polyps. The researchers speculate that there is a population of patients whose disease is exacerbated by *Staphylococcus aureus* enterotoxin.[4] Although doxycycline reduced polyp

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Abbreviation used
ECP- Eosinophilic cationic protein

size and symptoms only modestly, it supports the superantigen theory of chronic rhinosinusitis with nasal polyposis. The researchers speculate that doxycycline has great potential for extended use. Because of the modest effects observed, this trial does not support the use of doxycycline as monotherapy for nasal polyps. It does suggest that, in some patients, it might be an additive therapy to currently proven treatments such as nasal steroids.[5] Future studies will be needed to determine which patients with nasal polyps would benefit from the addition of doxycycline, what the best dosage schedule is, and whether there are additive or synergistic effects with other therapies. In particular, although both doxycycline and methylprednisolone decreased ECP, they had different effects on other inflammatory biomarkers, with doxycycline reducing matrix metalloproteinase-9 and myeloperoxidase, whereas methylprednisolone reduced IgE and IL-5. Because the 2 drugs seem to affect different inflammatory components, the hypothesis that they could result in additive or synergistic effects seems a reasonable one to test.

Future studies will be needed to determine which patients with nasal polyps would benefit from the addition of doxycycline, what the best dosage schedule is, and whether there are additive or synergistic effects with other therapies.

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